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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/282,239
Filing Date: March 31, 1999
Appellant(s): Goldman et al.

Michael Goldman
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 10/10/2006 appealing from the Office action mailed 1/24/2011.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal. Appellants noting that a prior Notice of Appeal to the Board of Patent Appeal and Interferences was filed on January 12, 2006 and subsequently withdrawn is acknowledged.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(**8) Evidence Relied Upon**

Rao et al., U.S. Patent No.: 6,361,996 B1.

Scherer et al. (Neuron Vol 12, pp 1363-1375, June 1994)

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 42-44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection of claims 42-44 under this statue remains because the recitation "...wherein 66.3 +/- 6.8% of cells in the enriched or purified preparation mature into O4-IR oligodendrocytes when cultured in the presence of 5% FBS/IGF-1." is not supported by appellants specification at the time of filing and is thus considered new matter. Specifically appellant's recitation of "preparation mature into O4-IR oligodendrocytes " is considered new matter. As previously stated in the office action of 3/10/2009, it would appear at best the only association that can be made with respect to 66.3 +/- 6.8% is "O4-IR cells". Support for anything beyond such is considered new matter, which includes "O4-IR oligodendrocytes".

Claim Rejections - 35 USC § 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 25, 26 and 29-41 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Rao et al. (U.S. Patent No. 6,361,996 B1) as evidenced by Scherer et al. (Neuron Vol 12, pp 1363-1375, June 1994).

Rao et al. teach an isolated, pure (enriched or purified) and homogeneous population of lineage-restricted oligodendrocyte-astrocyte precursor cells which are capable of self-renewal and differentiation into oligodendrocytes and astrocytes and methods of generating, isolating and culturing such oligodendrocyte-astrocyte precursor cells. The specific pure homogeneous population of cells isolated by Rao et al. is illustrated in Figure 1 (See specifically cell type –14, and the supporting text) and while Rao et al. specifically teach as an example said pure (enriched or purified) homogeneous preparation of cells as isolated from rat, Rao et al. point out that the invention encompasses all mammalian neuroepithelial stem cells and is not limited to neuroepithelial stem cells from the rat. Mammalian neuroepithelial stem cells can be isolated from human and non-human primates, equines, canines, felines, bovines,

porcines, ovines, lagomorphs, and the like. Thus, Rao et al. anticipates those claims to an enriched or purified preparation of human mitotic oligodendrocyte progenitor cells, wherein an oligodendrocyte specific promoter functions in all cells of the enriched or purified preparation.

The preparation taught by Rao is such that a cyclic nucleotide phosphodiesterase 2 promoter is inherently transcriptionally active in all cells of the enriched or purified preparation. This is evidenced by the reference Scherer et al. (Neuron Vol 12, pp 1363-1375, June 1994) who teach the differential cellular and temporal regulation of the 2',3'-cyclic nucleotide 3'-phosphodiesterase gene (CNP)and teach that the 2',3'-cyclic nucleotide 3'-phosphodiesterase II promoter is transcriptionally active in oligodendrocytes, Schwann cells and many additional tissues and appears before the appearance of mature oligodendrocytes, in oligodendrocyte precursor cells early in brain development (See page1365-1367, Figures 4 and 5 and supporting text).

Claims 25 and 26 which are drawn to the preparation of human mitotic oligodendrocyte progenitor cells are included in this rejection because these product-by-process like limitations ("from a post-natal human" for claim 25 and "from an adult human" for claim 26) do not change the oligodendrocyte progenitor cells of claim 29. Rao further teach that a better understanding of a number of tumors and other diseases in humans could be facilitated by a better understanding of these cell types and the ability to isolate and grow these mammalian cells *in vitro*, which allows for the possibility of using such stem cells to treat neurological disorders in mammals, particularly humans. Further, such mammalian neuroepithelial stem cells can be used

therapeutically for treatment of certain diseases, e.g. Parkinson's disease, such as by transplantation of such cells into an afflicted individual. Moreover, such cells can still further be used for the discovery of genes and drugs that are useful for treating certain of these diseases.

One of ordinary skill in the art at the time of filing would have been motivated to use the methods taught by Rao et al. to isolate an enriched or purified preparation of human mitotic oligodendrocyte progenitor cells from humans so that these pure cell preparations could be used to treat neurological disorders in humans, such as. Parkinson's disease, such as by transplantation of such cells into an afflicted individual. This motivation is suggested by Rao et al. and the reasonable expectation of success comes from the results of Rao et al. who successfully isolated such an enriched or purified preparation of mitotic oligodendrocyte progenitor cells from rat.

One of skill in the art at the time of filing would have been further motivated to isolate as an enriched or purified preparation, that cell identified in Example 7 of Rao et al. , i.e. those cells identified as "GalC immunoreactive cells could be seen, which cells also expressed A2B5 immunoreactivity" and not having the characteristic morphology of oligodendrocyte-type 2-astrocyte (O2A) progenitors or mature oligodendrocytes. These cells appeared after longer periods in culture and allowed more mature-looking oligodendrocytes with a small body and extensive processes to develop. These cells expressed O1 and GalC immunoreactivity, markers characteristic of differentiated oligodendrocytes. These cells which "appeared flattened and did not have the characteristic morphology of oligodendrocyte-type 2-astrocyte (O2A) progenitors or

mature oligodendrocytes" are evidence of the existence of an intermediate between cell type 14 and cell type 18 of Figure 1. As stated by Rao et al., the pattern of antigen expression further suggests the existence of a dividing oligodendrocyte precursor that subsequently generates oligodendrocytes, as has been described from spinal cord cultures from older embryos. The expectation of success is high given the results of Rao et al. who identify these cells and provide a source of their further enrichment and purification.

Given the importance in isolating oligodendrocyte progenitor cells to the understanding of how multipotent neuroepithelial stem cells become restricted to the various neuroepithelial derivatives, one of skill in the art would have been motivated to isolate the cells identified by Rao et al. which "appeared flattened and did not have the characteristic morphology of oligodendrocyte-type 2-astrocyte (O2A) progenitors or mature oligodendrocytes. One would have been motivated to isolate these cells as a means of understanding how multipotent neuroepithelial stem cells become restricted to the various neuroepithelial derivatives and in order to understand neuroepitheal disorders in human and to treat neurological disorders in mammals, particularly humans and the treatment of certain diseases, e.g. Parkinson's Disease, are evidence of the existence of an intermediate between cell type 14 and cell type 18 of Figure 1. As stated by Rao et al., the pattern of antigen expression further suggests the existence of a dividing oligodendrocyte precursor that subsequently generates oligodendrocytes, as has been described from spinal cord cultures from older embryos. The expectation of success is high based upon the high degree of knowledge in the art and the results and

expertise of Rao et al. who demonstrate the successful isolation of various cell types along the neuroepitheal development pathway.

For these reasons, claims 25, 26 and 29-41 remain rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Rao et al. (U.S. Patent No. 6,361,996 B1) as evidenced by Scherer et al. (Neuron Vol 12, pp 1363-1375, June 1994).

(10) Response to Argument

Claim Rejections - 35 USC § 112

Appellant's traversal of the rejection based upon new matter is acknowledged and it is pointed out that this rejection is made in the context of Appellants specification at the time of filing as well as the knowledge in the art. The rejection is based upon appellants reference to a subgenus of enriched or purified preparations wherein 66.3 +/- 6.8% of the cells in the in the enriched or purified preparation mature into O4-IR oligodendrocytes when cultured in the presence of 5% FBS.IGF-1.

Appellants traversal of this rejection is on the basis that Appellants submit that in Example 6, appellants submit that "P/hCNP2 :hGFP^{+} -sorted Cells Matured Largely, but not Exclusively, into Oligodendrocytes" is appreciated but not found persuasive on the basis that by appellants own submission these cells matured largely, but not exclusively into oligodendrocytes. While appellants submit that the specification notes "[b]y 3 weeks after FACS [(i.e. fluorescence-activated cell sorting)], 74.1 + 7.7% of these cells expressed oligodendrocytic CNP protein; a matched sample of sorted cells stained after

3 weeks *in vitro* for 04 yielded 66.3 + 6.8% O4-IR cells", appellants specification follows by noting of these "Nonetheless, concurrent development of non-oligodendrocytic phenotypes was also noted after FACS purification. Thus given the complexities of the art and appellants experiments and drawn conclusions, the only certainty is that 66.3+/- 6.8% of the cells were O4-IR positive. Not O4-IR oligodendrocytes.

With regard to Appellants submission that in the present application oligodendrocytes are 04 positive, this is not found persuasive in supporting appellants claim to the recited subgenus of preparations in which 66.3 +/- 6.8% of the cells in the in the enriched or purified preparation mature into O4-IR oligodendrocytes. As previously stated, if anything appellants specification may support the subgenus of preparations in which 66.3 +/- 6.8% of the cells in the in the enriched or purified preparation mature into O4-IR cells.

While appellants would appear to argue that the existence of the O4 antigen is synonymous with a cell being an oligodendrocyte, such is not clear in the art. Appellants attention is directed to Figure 2 of Rao et al. (U.S. Patent No. 6,361,996 B1 and presented on page 11 of Appellants Appeal Brief) which indicates the presence of a cell labeled as an oligodendrocyte which is presumably derived from a O-A progenitor and which may or may not express O4, as indicated by "O4+/-". Further, in support of this art recognized position, Appellants are directed to Rao et al. (U.S. Patent No. 6,361,996 B1, column 7, lines 45-67, in which they teach that Schwann cells, which are not oligodendrocytes, also express markers such as O4. Thus, contrary to Appellants position, there is not a clear understanding that expression of the O4 antigen is

associated with only oligodendrocytes and no other cell type. Thus appellants recitation of a subgenus of enriched preparations such that 66.3 +/- 6.8% of the cells in the in the enriched or purified preparation mature into O4-IR cells, does not support the subgenus of enriched preparations such that 66.3 +/- 6.8% of the cells in the enriched or purified preparation mature into O4-IR "oligodendrocytes".

Claim Rejections - 35 USC § 102/103

Appellants traverse the current rejection of claims 25, 26 and 29-41 under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Rao et al. (U.S. Patent No. 6,361,996 B1) as evidenced by Scherer et al. (Neuron Vol 12, pp 1363-1375, June 1994).

After a review of the applicable law (i.e. 35 U.S.C. 102(e) and 35 U.S.C. 103(a)), appellants traverse the rejection on the following basis:

Appellants submit that the rejection of claims 25, 26, and 29 Under 35 U.S.C. 102(e) as anticipated by or, in the alternative under 35 U.S.C.(l03(a) for obviousness over the Rao et al. (referred to by appellants as the '996 patent) is improper. In supporting appellants position appellants first present a considerable amount of background supporting the significance of and illustrating the need of appellants claimed invention. While this information is certainly of interest it is of minimal use if any in supporting appellants position that the current rejection should be withdrawn.

Appellants describe the '996 patent as disclosing multipotential neuroepithelial stem cells and lineage-restricted astrocyte/oligodendrocyte precursor cells, with an emphasis on "multipotential intermediate precursor cells restricted to glial lineages". Appellants further point out that the portion of the '996 patent relied upon for the rejection is Figure 1, and the supporting text regarding cell type 14, which is the referred to "multipotential precursor cell" that can generate oligodendrocytes 18 and astrocytes 22. It is further noted by appellants that the '996 patent experimental work was with rat cells, although it is acknowledged that the previous office actions have asserted that human cells could likewise be isolated and presumably used to produce human multipotential precursors of both oligodendrocytes and astrocytes. Appellants submit that even if such was true, one is still left to speculate how the '996 patent teaches the oligodendrocyte-specified progenitor cells of the claimed invention, noting the only possible bases for taking such a position are 1) explicit anticipation, 2) inherent anticipation and 3) obviousness. Appellants note that the '996 patent is not sufficient on any of these grounds.

Appellants submit that the '996 patent does not explicitly anticipate the claimed invention. Appellants continue to submit that nowhere does the '996 patent disclose the claimed enriched or purified preparations of human mitotic oligodendrocyte-specified and oligodendrocyte progenitor cells. Appellants submit that the astrocyte/oligodendrocyte precursor cells disclosed in the '996 patent are different from the oligodendrocyte-specified and oligodendrocyte progenitor cells claimed in the

present application and present the Declarations of Mahendra S. Rao, M.D., PH.D. in support of this position.

Appellants submit that declarant Mahendra S. Rao, the same Dr. Rao who is co-inventor of the '996 patent, has stated that the '996 patent's astrocyte/oligodendrocyte precursor cells are in a less differentiated state than the oligodendrocyte progenitor cells claimed in the present patent application. Furthermore, appellants submit Dr. Rao's publication Multipotent Neuroepithelial Stem Cells," Devel. Biol. 188:48-63 (1997) as demonstrating that such A2B5+mCAM- cells are capable of generating both astrocytes and oligodendrocytes and do not appear committed to the oligodendrocyte lineage.

Appellants submit that as shown in Figures 1-2 of the '996 patent, the astrocyte/oligodendrocyte precursor cells 14 and 54, respectively, differentiate directly into two cell types of astrocytes and oligodendrocytes and it is known from clonal analysis that there is a homogenous population of astrocyte/oligodendrocyte precursor cells in which individual cells generate oligodendrocytes and two kinds of astrocytes by the process described in the '996 patent.

Appellants further submit that it is important to note that multiple pathways to generate post-mitotic, mature oligodendrocytes, have been described, as well as the existence of other kinds of oligodendrocyte progenitors.

Appellants above arguments regarding what Rao et al. teaches and how this compares to appellants claimed invention continue to be acknowledged, as stated in the previous rejections and repeated herein.

First, it is noted that appellants distinction between the "multipotential neuroepithelial stem cells and lineage-restricted astrocyte/oligodendrocyte precursor cells" of Rao et al., as characterized by appellants and that of the "oligodendrocyte-specified progenitor cells" of the appellants claims while acknowledged, remains unclear and confusing. It remains that the claimed "oligodendrocyte-specified progenitor cells" do not by definition exclude those progenitor cells which may differentiate to cells other then oligodendrocytes. By its broadest reasonable interpretation, it continues that an "oligodendrocyte-specified progenitor cell" is interpreted as any progenitor cell which is specified to give rise to an oligodendrocyte. This reasonable interpretation does not exclude those progenitor cells that give rise to additional related cell types such as astrocytes. Thus this includes unipotential, as well as bi- and multi-potential cells. Given this interpretation, the "multipotential neuroepithelial stem cells and lineage-restricted astrocyte/oligodendrocyte precursor cells" taught by Rao et al. and exemplified by Rao et al. in Figure 1, as cell type 14, are considered to be encompassed by an "oligodendrocyte-specified progenitor cell". As these cells are further mitotically active these cells are "mitotic oligodendrocyte-specified progenitor cells".

With respect to appellants submission that nowhere does the '996 patent disclose the claimed enriched or purified preparations of mitotic oligodendrocyte-specified and oligodendrocyte progenitor cells, appellants are reminded that the majority of those preparations of Rao et al. are "enriched or purified" as such does not require a

specific degree of "enrichment or purity", but merely some "enrichment or purity" as is disclosed by Rao et al. in most of the examples, such as example 7.

Not withstanding the above broadest reasonable interpretation of an oligodendrocyte-specified progenitor cell, if one was to consider that appellants claims were directed to an oligodendrocyte-specified progenitor cell which is "unipotential" such that it only gives rise to oligodendrocyte cells and not to other types of cells, such as astrocytes, then this "further specified oligodendrocyte-specified progenitor cell" would also be anticipated by Rao et al. in its preparations of examples 15 and 7. Each of these example preparations start with NEP-derived A2B5+ cells and allow these progenitors to develop to oligodendrocytes. Thus, the NEP cells differentiated to cell type 14 (as per Figure 1) and further differentiated to cell type 18 (as per Figure 1). Thus an intermediate between the cell type 14 and 18 must have existed in the preparations of Examples 15 and 7.

Relative to such an argument, appellants submit that Dr. Rao is not aware of any evidence that the astrocyte/oligodendrocyte precursor cells of the '996 patent generated mature oligodendrocytes by way of an intermediate oligodendrocyte-specific precursor and appellants further present Gregori et al., J Neurosci. 22(1):248-256 (2002) as suggesting that the '996 patent describes a glial progenitor that gives rise to a more restricted astrocyte/oligodendrocyte precursor that still directly makes predominantly astrocytes and a small minority of oligodendrocytes. Thus, cells in the '996 patent's pathway to oligodendrocyte production are bi- potential astrocyte/oligodendrocyte progenitor cells that have strong astrocytic bias. 'Appellants continue to submit that

these cell types are very different from the claimed oligodendrocyte-specified progenitor cells of the present application.

In response to this argument, appellant is again reminded that as discussed above, by its broadest reasonable interpretation, it continues that an "oligodendrocyte-specified progenitor cell" is interpreted as any progenitor cell which is specified to give rise to an oligodendrocyte and this includes unipotential as well as bi- and multi-potential cells, such as that taught by Rao et al. in Figure 1, as cell type 14. If as discussed above for the sake of argument, one was to consider that the claimed progenitor cell must be unipotential, such that it only differentiated into an oligodendrocyte cell, (that is an intermediate between cell type 14 and cell type 18) then contrary to the declaration of Dr. Rao, there is evidence of the existence of such a cell type. This evidence is found in Example 7 of the Rao et al. patent.

As demonstrated in example 7 of Rao et al., NEP cells grown on fibronectin in NEP medium for 5 days according to the procedure of Example 1 were harvested by trypsinization and replated on laminin-coated plates in neuroepithelial culture (NEP) medium without the addition of CEE for 5-10 days. Differentiating NEP cells were then labeled, according to the procedure of Example 4, with markers previously identified as being expressed on oligodendrocytes and their precursors: A2B5, GalC, O1, and O4. Three days after replating NEP cells, a subset of the cells began to express A2B5 immunoreactivity. A2B5 immunoreactive cells initially did not express detectable levels of GalC, O4, and O1 immunoreactivity. These cells correspond to the Figure 1, cell type 14 . After an additional three days in culture, however, "GalC immunoreactive cells

could be seen, which cells also expressed A2B5 immunoreactivity". Such cells appeared flattened and did not have the characteristic morphology of oligodendrocyte-type 2-astrocyte (O2A) progenitors or mature oligodendrocytes. Longer periods in culture, however, allowed more mature-looking oligodendrocytes with a small body and extensive processes to develop. These cells expressed O1 and GalC immunoreactivity, markers characteristic of differentiated oligodendrocytes. These cells which "appeared flattened and did not have the characteristic morphology of oligodendrocyte-type 2-astrocyte (O2A) progenitors or mature oligodendrocytes" are evidence of the existence of an intermediate between cell type 14 and cell type 18 of Figure 1. As stated by Rao et al., the pattern of antigen expression further suggests the existence of a dividing oligodendrocyte precursor that subsequently generates oligodendrocytes, as has been described from spinal cord cultures from older embryos.

Appellants further submit that example 15 of the '996 patent specifically conducts work to investigate whether mature astrocytes and oligodendrocytes are generated from committed unipotential cells present in the A2B5+ population of cells (i.e. cell types 14 and 54 in Figures 1 and 2, respectively) or whether single cells are bipotential and can generate both astrocytes or oligodendrocytes and concludes that the A2B5+ cells were at least bipotential and were restricted to glial cell lineages. Thus appellants conclude that '996 patent not only fails to disclose the claimed oligodendrocyte-specified progenitor cells but teaches away from their presence. This argument is acknowledged, however, appellants drawn conclusion that "the A2B5+ cells were at least bipotential and were restricted to glial cell lineages" is not inconsistent with the existence of an

intermediate A2B5+ cell between cell type 14 and cell type 18, as supported by the above discussion of example 7.

Appellants' argue that the examiner's previous statements that appellants are arguing differences between the '996 patent disclosure and the disclosure of the present application, not the claims of the present application, is in error based upon appellants position that the '996 patent fails to teach oligodendrocyte-specified progenitor cells and this is precisely what appellants are claiming. For the reasons discussed above, Rao et al. does teach oligodendrocyte-specified progenitor cells. It appears that much of appellants above argument is based upon characteristics of the cells taught by Rao et al. (i.e. bipotentiality) which appellants argue are not characteristics of appellants cells. Appellants appear to be arguing "characteristics" or "limitations" of the claims which do not exist.

Appellants further argue that in addition to failing to teach the claimed oligodendrocyte progenitor cells, the '996 patent also worked with cells from rats rather than from humans, as required by the claimed invention and that there are fundamental differences between the biology of rat and human oligodendrocyte progenitor cells (Declaration of Steven A. Goldman Under 37 C.F.R. 1.132, First Goldman Declaration") and there are fundamental differences between the lineage restriction and potential of neonatal and adult oligodendrocyte progenitor cells.

Appellants submit that these biological differences between both rat and human and perinatal and adult progenitor cells were not recognized by the '996 patent, whose cells were restricted to neonatal rodent derivation. Appellants submit that whereas rat

oligodendrocytes appear to retain mitotic potential, human oligodendrocytes do not and as a result, the oligodendrocyte progenitor cells of the rat brain cannot be considered homologous to its human counterpart.

Appellants argument that certain cell populations between species have differences is appreciated, however not found persuasive relative to the teachings of Rao et al. and how these relate to the claimed invention. As previously stated, the enriched or purified homogeneous population of cells isolated by Rao et al. as illustrated in Figure 1 (See specifically cell type –14, and the supporting text) in the examples section of Rao et al. are isolated from rat, and Rao et al. point out, however, that the invention encompasses all mammalian neuroepithelial stem cells and is not limited to neuroepithelial stem cells from the rat. Rao et al. specifically teach that mammalian neuroepithelial stem cells can be isolated from human and non-human primates, equines, canines, felines, bovines, porcines, ovines, lagomorphs, and the like. Thus while Rao et al. use rat cultures as an example of the taught mammalian neuroepithelial stem cells, they teach said neuroepithelial stem cells from human and non-human primates, equines, canines, felines, bovines, porcines, ovines, lagomorphs, and the like. None of the supposed differences between rat and human neuroepithelial cells as argued by appellants have any bearing to the taught oligodendrocyte-specified progenitor cells, whether they are from human or rat.

With respect to appellants argued differences between the lineage restriction and potential of neonatal and adult oligodendrocyte progenitor cells, appellants are reminded that such differences are considered irrelevant to the teachings of Rao et al.

and the claimed invention. It is noted that appellant's claims are directed to those oligodendrocyte progenitor cells (See above discussion regarding the broadest reasonable interpretation of such cells) from "post-natal" or an "adult" and the relationship of these "limitations" to each other are somewhat confusing. Not withstanding that, adults are considered to be "post-natal", that is adult-hood occurs subsequent to birth or natal, it remains that the relative limitations of the claimed cell populations as a result of being from "post-natal" or from "adult" are unclear. Further it is noted by Rao et al. that "oligodendrocytes appear later and are first detected around birth though oligodendrocyte precursors may be present as early as E14…". As stated by Rao et al., the pattern of antigen expression of those cells analyzed in Example 7 above, further suggests the existence of a dividing oligodendrocyte precursor that subsequently generates oligodendrocytes, as has been described from spinal cord cultures from older embryos. This is more recognition of the existence of the above refuted cell types as well as support that such cells from earlier as well as older embryos and adults are the same.

Finally appellants argue that the methods used by Rao et al. that permit the selective extraction and/or growth of oligodendrocyte progenitors from the rat brain do not differentiate between oligodendrocyte progenitor cells and mature oligodendrocytes able to re-enter the mitotic cycle and in humans, these constitute two discrete phenotypes, lineally related but temporally distinct. Appellants point is acknowledged that the methods taught by appellant's specification are different from those taught by Rao et al., however, this is not considered relevant to the claimed "enriched or purified

preparation". Appellants are reminded that appellant's claims are merely drawn to enriched or purified preparations, and that such does not require that precursors to the claimed cells or cells that are derived from the claimed cells be removed from the preparations. It merely requires that the preparations of claimed "oligodendrocyte progenitor cells" be "enriched or purified" These preparations need not be "enriched and purified", but enriched or purified, and minimal enrichment or minimal purification would meet each of these limitations.

With respect to appellants arguments that the '996 patent does not inherently anticipate claims 25, 26, and 29-41, appellants submit that previously, in an interview, the examiner asserted that the '996 patent's multipotential oligodendrocyte-astrocyte precursor cells must inherently differentiate to the claimed oligodendrocyte-specified and oligodendrocyte progenitor cells before further differentiating to mature oligodendrocytes. Appellants submit that when a prior art rejection is based on the inherent characteristics of a claimed product, as disclosed in the cited art, the examiner's burden for maintaining the rejection, and appellants' burden in rebutting this rejection, is well-defined. Appellants argue the examiner's inherency position by submitting evidence in the form of the Declarations by Dr. Rao in which they submit that they demonstrate that the astrocyte/oligodendrocyte precursor cells disclosed in the '996 patent are different from the oligodendrocyte- specified and oligodendrocyte progenitor cells claimed in the present application. Additionally, appellants continue to submit that the experimental work discussed in Example 15 of the '996 patent demonstrates that even when the inventors looked at the specific issue needed to

support an inherency position (i.e. whether the mature oligodendrocytes and astrocytes produced were from a unipotential or multipotential MB5+ cell population), they found that that population was multipotential.

In response to appellants position regarding any inherency issue, it remains that as discussed above, the rejection need not rely on inherency, as the claimed "oligodendrocyte progenitor cells" continue to be anticipated by the "enriched or purified" preparation of Rao et al. which comprises cell type 14 from figure 1 as shown in examples 7 and 15. Appellants continue to argue the difference between the "enriched or purified" preparations of Rao et al. and that of appellant's claims, however, as discussed repeatedly above, appellant's claims to "oligodendrocyte progenitor cells" do not include any limitation that excludes the cell type 14 of figure 1 of Rao et al. If it is evidence of the existence of an intermediate cell type between cell type 14 and a mature oligodendrocyte that appellant's request, as discussed above in example 7, of Rao et al., after an additional three days in culture, "GalC immunoreactive cells could be seen, which cells also expressed A2B5 immunoreactivity". Such cells appeared flattened and did not have the characteristic morphology of oligodendrocyte-type 2-astrocyte (O2A) progenitors **or** mature oligodendrocytes. Longer periods in culture, however, allowed more mature-looking oligodendrocytes with a small body and extensive processes to develop. These cells expressed O1 and GalC immunoreactivity, markers characteristic of differentiated oligodendrocytes. These cells which "appeared flattened and did not have the characteristic morphology of oligodendrocyte-type 2-

astrocyte (O2A) progenitors **or** mature oligodendrocytes" and are evidence of the existence of an intermediate between cell type 14 and cell type 18 of Figure 1.

With respect to appellants arguments regarding that the '996 patent does not render the invention of Claims 25, 26, and 29-41 obvious, appellants submit all that the '996 motivates those skilled in the art to do is find a preparation of bipotential oligodendrocyte-astrocyte precursor cells (i.e. cell type 14 of figure 1), not oligodendrocyte-specified progenitor cells, as claimed by appellants. Appellants submit that there is absolutely no suggestion in the '996 patent that there are oligodendrocyte-specified progenitor cells in rats (or any other species).

In response to such an argument, appellants are again reminded as discussed above, that the cell type 14 of figure 1 as taught by Rao et al. is considered to be an oligodendrocyte-specified progenitor cell. Thus appellants have admitted the motivation (if needed) to isolate such exists in the '996 patent.

Appellants arguments based upon "inherent teachings of the 996 patent" are acknowledged, however, not found persuasive on the basis that as discussed above, inherency is not needed to anticipate and/or make obvious the claimed "enriched or purified preparations of oligodendrocyte-specified progenitor cells".

Finally appellants arguments based upon appellants presented significance of appellants invention and teachings are acknowledged, however, not persuasive in overcoming the rejection for all of the reasons discussed previously and above.

Finally, appellants argue that the mitotic oligodendrocyte progenitor cells from an adult human of claim 26 are further distinguishable from the astrocyte/oligodendrocyte precursor cells of the '996 patent, on the basis that differences in the method, time of isolation, and propagation suggest a difference between the cell types of claim 26 and those disclosed in the '996 patent. Appellants submit that the cells of claim 26 of the present application were derived from the adult brain using a promoter reporter based strategy, while the '996 patent is directed to the enrichment of glial progenitor cells from newborn rat brain. Appellants are reminded that appellants claims are drawn to a preparation of cells, and not to methods and thus while the methods taught by Rao et al. and that of appellants specification may be different, the "enriched or purified preparations of oligodendrocyte-specified progenitor cells are considered to be the same. Appellants further submit that in contrast to adults, newborns have an abundant population of still-developing oligodendrocyte progenitor cells that may constitute a significant action of all of the cells in neonatal brain and appellants submit that adult-derived oligodendrocyte progenitor cells not only myelinate much more rapidly than do fetal oligodendrocyte progenitors, but they do so more efficiently, with a higher proportion exhibiting effective myelin production, and myelinating a greater number of neuronal axons per donor cell than their fetal-derived counterparts thus, adult oligodendrocyte progenitor cells are fundamentally different from fetal or neonatal-derived progenitors and, therefore, the '996 patent's rat fetal astrocyte/oligodendrocyte precursor cells are very different from the adult oligodendrocyte progenitor cells in claim 26 of the present application.

Appellants complete argument regarding the differences between the cells of Rao et al. and that of appellants claims continue to be acknowledged, however, it remains that the cell preparations of appellants are anticipated by the cell preparations taught by Rao et al., regardless of the source or stage of organism from which the cell is from, as the cells are the same. The oligodendrocyte specified progenitor cells taught by Rao et al. are the same whether they are from a neonate or an adult organism. An oligodendrocyte-specified progenitor cell is an oligodendrocyte-specified progenitor cell.

Finally, given the importance in isolating oligodendrocyte progenitor cells to the understanding of how multipotent neuroepithelial stem cells become restricted to the various neuroepithelial derivatives, one of skill in the art would have been motivated to isolate the cells identified by Rao et al. which "appeared flattened and did not have the characteristic morphology of oligodendrocyte-type 2-astrocyte (O2A) progenitors or mature oligodendrocytes. One would have been motivated to isolate these cells as a means of understanding how multipotent neuroepithelial stem cells become restricted to the various neuroepithelial derivatives and in order to understand neuroepitheal disorders in human and to treat neurological disorders in mammals, particularly humans and the treatment of certain diseases, e.g. Parkinson's Disease, are evidence of the existence of an intermediate between cell type 14 and cell type 18 of Figure 1. As stated by Rao et al., the pattern of antigen expression further suggests the existence of a dividing oligodendrocyte precursor that subsequently generates oligodendrocytes, as has been described from spinal cord cultures from older embryos. The expectation of success is high based upon the high degree of knowledge in the art and the results and

expertise of Rao et al. who demonstrate the successful isolation of various cell types along the neuroepitheal development pathway.

For these reasons, claims 25, 26 and 29-41 remain rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Rao et al. (U.S. Patent No. 6,361,996 B1) as evidenced by Scherer et al. (Neuron Vol 12, pp 1363-1375, June 1994, see appellants IDS).

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(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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